

# Spatio-Temporal Study of Gastric Cancer Incidence in Kermanshah Province, Iran During the Years 2009-2014

Abozar Solimany<sup>1</sup>, Malihe Khoramdad<sup>2\*</sup>, Nahid Khademi<sup>1</sup>, Ali Delpisheh<sup>3</sup>

## Abstract

**Background and objective:** Stomach cancer is the second common and the most deadly type of cancer in Iranian populations. The pattern of this cancer varies in different populations; demonstrating association with environmental, racial, and geographical factors. The focus of this study was to identify the clustering and the high-risk and low-risk regions for stomach cancer by using spatio-temporal analysis in Kermanshah province during 2009-2014. **Method:** All new cases of stomach cancer were studied by census method in 2009 to end 2014 in Kermanshah province. The required information and statistics (address, age, and sex) of patients were extracted from the cancer registry system of Vice-Chancellor in health affairs, Kermanshah University of Medical Sciences. Also, with having the location, diagnosis time, and counting information of all age groups of stomach cancer patients, the spatially and temporally abnormal places of clustering were identified with the use of saTScan and GIS. **Results:** the total number of stomach cancer subjects during the period of study was 1040, with a mean age of  $66.5 \pm 1$ . In addition, 11 regions (located in 1<sup>st</sup>, 2<sup>nd</sup>, and 3<sup>rd</sup> municipal districts) demonstrated abnormal Spatio-temporal pattern of stomach cancer incidence (hot spots) and clustered disease, with 5 regions (in 4<sup>th</sup> and 5<sup>th</sup> districts) representing lower chance of clustering (cold spots,  $p$  value < 0.05). **Conclusion:** Given the growing rate of stomach cancer incidence in specific geographical areas and, its high potential of mortality, and the possible relationship with environmental variables (e.g. climate variables); the efforts need to be focused on the identification of hot/cold spots, the predisposing factors, and the possible clusters in the affected areas.

**Keywords:** Stomach cancer- clustering of disease- hot-spots- cold-spots- Spatio-temporal analysis

*Asian Pac J Cancer Prev*, **19** (10), 2871-2876

## Introduction

Since the groundbreaking advances in medical sciences have led to the harnessing of infectious diseases, non-infectious diseases, e.g. cancers, have attracted a much more attention in societies (Rafti et al., 2008). According to the WHO report, Cancer is the second major cause of death worldwide, with being culprit of 8.8 million death in 2015 (WHO, 2018). It also is the third most common known cause of death in Iran, after cardiovascular diseases and accidents (Sadjadi et al., 2003). Among different types of this disaster, upper gastrointestinal tract cancers; especially stomach cancer, have posed a considerable threat in developing countries (Murray and Lopez, 1997). In respect to the report of the International Agency for Research on Cancer (IARC) in 2012, gastric cancer is the fifth most common cancer in the world. It is third cause of cancer mortality in both sexes worldwide. Moreover, in 2012 in Iran, gastric cancer was responsible for 11.4% of all cases of cancer occurrence and was considered as the second most prevalent cancer. In the same year, gastric

cancer with taking part in 15.5 percent of all cancer-caused mortalities caused by cancers, was in fact the most deadly cancer in Iran (International Agency for Research on Cancer, 2018). Stomach cancer was also shown to be the fourth common type of cancer in Kermanshah province (in women: after the breast cancer, skin cancer, and colon cancer; in men: after skin cancer, bladder cancer, and colon cancer) (Etemad et al., 2012)

Various studies have been done to discern risk factors for different cancers around the world, indicating that the incidence of cancers correlate with racial, geographical, and environmental conditions, inasmuch as there is an obvious variation in prevalence and frequency of various cancers in different areas (Enayatrad and Salehiniya, 2014). The heterogeneity of stomach cancer in different areas of the world have shown that the stomach cancer is mostly affected by environmental factors, which can also be accounted for variations observed in Iran (Mohagheghi et al., 2009). Notably, the highest rate of stomach cancer among Iranian society was reported in Mazandaran, Golestan, and Ardabil, with the lowest rate

<sup>1</sup>Faculty of Health, Kermanshah University of Medical Sciences, Kermanshah, <sup>2</sup>Student Research Committee, Faculty of Public Health Branch, Iran University of Medical Sciences, Tehran, <sup>3</sup>Department of Epidemiology, Ilam University of Medical Sciences, Ilam, Iran. \*For Correspondence: m.khoramdad2016@gmail.com

in south and southwest provinces, especially Kerman (Malekzadeh et al., 2009).

In the analysis of stomach cancer incidence in migrants (as the key components of epidemiological studies), adjustment with the overall population of migrant sending and receiving countries demonstrates the role of environmental factors in stomach cancer. As an evidence, there has been a sharp decline in both esophagus and stomach cancer in Iranian residences of Canada (Stracci et al., 2007). With this in mind, it should be stressed that the recording of disease separately in different geographical regions will allow the testing of variable patterns of disease, paving the way for the identification of high risk and low risk areas (Liu-Mares et al., 2013).

A newly developed branch of epidemiology, Field Epidemiology, has currently attracted particular attention. One of the research focuses in this new field is the exploration of clustering of health-related events. Diseases cluster is defined as a group of events in a geographical area which has a high numerical and cumulative frequency that rules out the possibility of stochastic occurrence. On the other hand, if the clustering of diseases occur in a specific place, it would be referred to as "spatial clustering", which could be observed in rarely happened events, like suicide, abortion, and cancers. Moreover, there is another type of clustering called time-space clustering, which includes both spatial and temporal aspects. The latter emphasize that the incidence rate of diseases is higher in specific areas, which in turn varies with the time. In fact, clustering analyses could be etiologically worthwhile, owing to the possibility of false clustering in both traditional and simple clustering approaches. Therefore, by using a currently developed approach, explorative statistics, insignificant clusters can be identified.

The focus of this study was to identify the clustering and the high-risk and low-risk regions for stomach cancer by using spatio-temporal analysis in Kermanshah province during 2009-2014.

## Materials and Methods

This ecological study was conducted in Kermanshah, a province with 24,640 km<sup>2</sup> area (1.5% of total area of Iran), located in west Iran. According to the statistical annals of 2012, the population of this province was 1,945,227, including 14 counties, 31 urban districts, 86 rural districts and 32 cities (Figure1).

In this study, all new cases of stomach cancer were studied by census method in 2009 to end 2014 in Kermanshah province. The required information and statistics (address, age, and sex) of patients were extracted from the cancer registry system of Vice-Chancellor in health affairs, Kermanshah University of Medical Sciences. This registry system is based on the population-based cancer reporting system. A team consisted of one pathologist and two laboratory technician who monthly collect the diagnostic reports of 22 pathology laboratories and 3 cancer centers of Kermanshah province. Under supervision of pathologists and after repeated measures, data are entered into the software, with adjusting them with the information of

total cancer patients around the country. Eventually, data are completed with additional repeating measurements and recording the new cases.

With taking into account data being numerical and discrete in cases of rare diseases (e.g. cancers), it is thought that there is a Poisson distribution pattern for the number of patients in each region. For identification of regions with remarkably higher number of patients than expected, spatial scan statistics can be used. Through this method, the estimation of equality of disease inside and outside of the cluster versus the estimation of higher risk inside the cluster would be explored. Next, the high risk in cluster is identified regarding the maximum logarithm likelihood ratio. Space-time statistics is a general form of spatial scan statistics which is exemplified as a person who have a cylinder-like window with a circle-shaped base and time-corresponding height. The position of this window changes with varying time and space in all parts of the country, including all likely intervals in time that could be found from the beginning of the study for the occurrence of a disease. The importance of a specific disease determine the size of scan window, which in this study was estimated to be 50% of the total at risk population.

Data were entered into an excel file and used to obtain the crude rate of data of census in 2005 and 2011. Furthermore, direct standardization based on Standard population table designed by World Health Organization (WHO) was used to eliminate the effects of age and sex (Ahmad et al., 2001). In this study, with having the location, diagnosis time, and counting information of all age groups of stomach cancer patients in Kermanshah, the spatially and temporally abnormal places of clustering were identified with the use of saTScan (version 9.4) and GIS (version 9). The output of software was in both forms of textual and GIS-based SHP formats which along with textual analysis of location, time, affected population, incidence rate, and relative risk, could be used to observe the high/low risk areas, the width of cluster, and the urban and rural areas within the cluster.

## Results

The total number of patients with stomach cancer in Kermanshah from 2009 to 2014 was 1040 individuals aged 12 to 98 years (733 (70.5%): men vs. 307: women (29.5%)). The age mean of patients was 66.5±13 years (67.6±12 in men and 63±13 in woman). Finally, 75% of total patients lived in urban areas and others in rural areas.

In this period, the highest crude stomach cancer rate in the total population of Kermanshah was reported in 75-79 years old patients (75-79 years old in men vs. 74-75 years old in women). The average annual incidence was 8.8 per 100,000 cases, with 6-year incidence being 46.1 per 100,000 (63.6 in men vs. 28.2 in women). Furthermore, the highest standardized rate was reported in Kermanshah County, while in Gilan-e Gharb County (Table 1). Also age-standardized incidence rate of stomach cancer showed incidence rate in men is higher than female (Table 2). that this association was significant ( $p < 0.005$ ). In addition, there was a meaningful difference between the incidence of stomach cancer and location

Table 1. Age-standardized Incidence Rate of Stomach Cancer in Different Counties of Kermanshah Province During 2009-2014

County	eslamabad	Pave	Salas	javanrood	Dalahoo	ravansar	sarpol	Songhor	Sahneh	Ghasr	kermanshah	kangavar	Gilan	harsin
Number of cases in 6 years	65	25	12	27	13	15	29	44	32	8	662	37	11	60
Crude incidence in 6 years	33	31.6	25.9	32.2	27.6	25.8	26.8	41.3	35.2	19.6	56	37	9.5	53.3
Total Standardized incidence rate	35.6	37	40.1	53.1	26.2	32	37.7	39.3	33.6	25.4	66.6	40.7	24.3	59.5

Table 2. The Sex-based Standardized Incidence Rate of Stomach Cancer in Kermanshah Province During 2009-2014

Years	2009		2010		2011		2012		2013		2014	
Sex	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Crude incidence rate	10.9	5.3	15	7.5	15.5	6.7	11.9	5.8	11.3	3.9	11	3.7
Standardized incidence rate	14.7	7.4	20.2	10.6	20.3	6.6	16.5	8	16.6	5.1	13	4
Total Crude incidence rate	8.2		11.1		10.9		8.7		7.5		6.1	
Total Standardized incidence rate	15.2		19.4		20.4		14.8		12.2		13	

Table 3. Spatiotemporal Analysis of High risk and Low Risk Areas for Stomach Cancer in Kermanshah Province (2009-2014)

Cluster Number	1	2	3	4	5
Time Cluster	2010/01/01 2011/12/29	2009/01/01 2012/12/09	2010/01/01 2012/12/29	2009/01/01 2013/12/29	2009/01/01 2013/12/29
Affected areas	Kermanshah Harsin, bistoan, Mahidasht Sarfiroozabad	Poshtdarband, bilavar, dinavar	Songhor, kolyaie, satr	Ghasreshirin, sarpolezahab, Ezgleh	Gilangharb, haidarieh
Population cluster	1,279,597	65,542	75,879	112,523	74,703
Number of cases	539	42	67	7	6
Expected number	341	18	38	29	9
Annual incidence	8.4	12.1	17.5	1.2	1.6
Observed/ expected	1.6	2.3	1.75	0.25	0.6
Relative risk clusters CI%95	2.04 (1.8-2.4)	1.9 (1.6-2.3)	1.83 (1.5-2.1)	0.7 (0.5-0.9)	0.4 (0.3-0.8)
Log likelihood ratio	21.8	12.7	11.3	12.4	14.4
P-value	<0.05				



Figure 1. Location of Kermanshah Province in Iran

(urban or rural areas), inasmuch as the incidence was remarkably higher in rural areas.

Following spatio-temporal analysis, 5 low-risk and high-risk clusters with a p-value<0.05 were identified. In total, 11 districts within three high-risk clusters (clusters 1, 2, and 3) were suggested as the areas where the incidence of stomach cancer has an unusual pattern of stomach cancer both in term of spatial and temporal difference of each cancer cases and were considered as the hot-spot areas. In contrast, there were 5 districts in clusters 4 and 5 with lower possibility of formation of stomach cancer clusters based on the spatial pattern of incidence (cold-spot areas) (Figure 2).

In Spatio-temporal analysis, besides the location factor which is solely analyzed in a majority of studies, another key factor was assessed in current study and the time difference of each cancer occurrence in a specific location was determined. Regarding the number of stomach cancer subjects and expected rate, their ratio, the log likelihood ratio in each cluster; and based on the relative risk in the same cluster in each area with

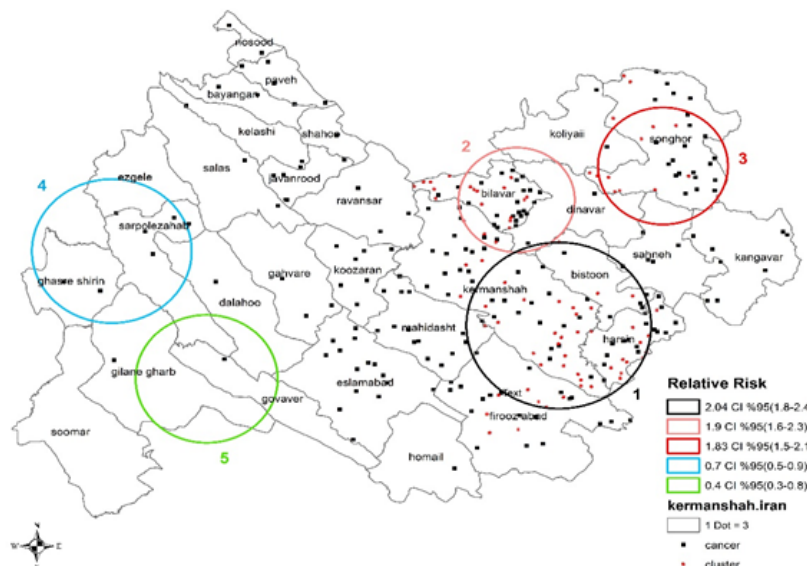


Figure 2. The Zoning of High Risk and Low Risk Areas of Kermanshah Province, Iran, During 2009-2014

p-value lower than 0.05, clusters were determined and zoned (Table 3). Considering the location, the high-risk and low-risk areas of Kermanshah province can be divided into 2 groups: 1) high-risk areas in the east including 1<sup>st</sup>, 2<sup>nd</sup>, and 3<sup>rd</sup> districts (height: >1,000 meters above sea level, 20-year average temperature: <15°C); and 2) low-risk areas in west including the 4<sup>th</sup> and 5<sup>th</sup> districts (height: <800 meters above sea level, 20-year temperature average: >20°C).

## Discussion

Global statistics have revealed that despite the remarkably decreasing trend of stomach cancer in European countries, e.g. Spain and Italy (Sheehan et al., 2004; Liu-Mares et al., 2013), the majority of developing countries are experiencing a growing rate of this type of cancer. For example, Mongolia (32.5 per 100,000), Tajikistan (21.7 per 100,000), Albania (20.1 per 100,000), Belarus (18.8 per 100,000), and Vietnam (16.3 per 100,000) have shown the highest rate of stomach cancer in the world (Pariona, 2017). This rate in Iran has been estimated 16.01 and 7.78 per 100,000 subjects in men and women, respectively (Ramezani Gourabi and Hanifi, 2011).

In Iran, the highest rate of stomach cancer is observed in south west provinces (Ardabil: 51.8 per 100,000) (Babaei et al., 2009), and this rate is increasing in the west. The standardized incidence rate in Kermanshah province has varied from 2.9/100,000 in 2009 to 7.9 in 2005. In addition, in other five western provinces the rate increased from 6.1 to 10.8 (Rahimi and Heidari, 2012). This increase was obvious in both genders, which may in part has to do with both the improvement of cancer recording system and change in risk factors. However, efforts failed to precisely identify the affected areas, groups, and potential risk factors for stomach cancer.

The results of current study showed that the highest rate of stomach cancer belonged to the 75-79 age group (men) and 70-74 age group (in women).

Besides, >70 and <20 years age populations were identified as the high-risk and low-risk groups, accordingly. Rahimi and Heidari, (2012) (in west Iran) and Babaei et al., (2009) (in Semnan) have reported similar results in 2005. The mean diagnosis age of stomach cancer in Kermanshah is 69 years, which is the reason for the lower survival rate for patients in this province. Early diagnosis of stomach cancer plays a key role in better response to therapy and higher survival rate. Notably, the incidence of stomach cancer in united states subjects with > 65 years age is 5-times higher than that of middle-age patients, with an incidence in men two times higher than women (Baranovsky and Myers, 1986; Fang et al., 2004).

In a large number of infectious diseases, owing to the identified infectious agent, clear period of contagiousness and incubation; it is easier to identify the irregular incidence of such diseases. First, non-infectious diseases do not have a unique causal agent (multi-factorial). Second, the exposure time is not fully clear. Third, we are unaware of the onset, latent, and incubation time of non-infectious diseases. Routine epidemiological studies to a great extent can be used to determine the volume of affected subjects, high-risk groups, and helpful preventive strategies. Conversely, owing to the vague and progressive nature of non-infectious diseases, the first and foremost action is to determine whether an epidemic occurred or not, followed by identification of influenced areas and potential influential factors. Spatio-temporal analysis is a promising tool to achieve this objective, which is a novel statistical and epidemiological method and is being widely used for both infectious and non-infectious diseases around the world.

Among the first studies on the early identification of clustering in stomach cancer, Hjalmar et al. study on pediatric leukemia in 1996 can be mentioned. They failed to identify any remarkable cluster in this group of patients by spatial analysis (Hjalmar et al., 1996). Aragonés et al. reported a declining rate of stomach cancer in Spanish population (Nuria et al., 2013). Similarly,

Papoila et al. showed a negligible distribution of this cancer (except in south) in Portuguese population (Papoila et al., 2014). Also in an Italian spatio-temporal study, the high-risk areas for stomach cancer (areas with a >1 relative risk) were determined by Mancini et al (Mancini et al., 2015). Recently, a couple of studies have been conducted on Iranian population, focusing on the zoning of stomach cancer. Asmarian et al. marked south and south west parts of Iran as the high risk areas in 2007 (Asmarian et al., (2012). Kavousi et al., (2014) highlighted that the south, south west provinces (Ardabil, Kurdistan, Mazandaran, and Gilan) had the greatest distribution of stomach cancer. However, they did not include the Kermanshah province in the high-risk group.

It should be emphasized that the proper determination of high-risk populations for an event which can affect the health system in an area is of particular importance. In the majority of Iranian studies, the whole population of a specific province has been classified in the high-risk group, without considering the climate variations which can be extremely different even between cities with a low distance. These variations can remarkably affect the incidence of a wide variety of diseases. In the current study, through Spatio-temporal analysis, we detected 118 spots with high standardized rate of incidence in Kermanshah province, which was even greater than other high-risk provinces of Iran. The procedure of our study was based on the standardized rates and their association with the geography of a specific location. The occurrence, identification time, the location of patients and their spatial and temporal distance were analyzed and it was found that in eastern areas of Kermanshah (mountainous areas), clustering of stomach cancer occurred, while the chance of clustering in tropical areas of this province was substantially low.

The exploration of geographical distribution and epidemiological zoning for stomach cancer is absolutely essential not only for research purposes, but for more appropriate funding in health. Zoning of the disease in each area paves the way to precisely determine the etiology and the geographical weighting, as well as provides the health policy authorities with a guideline to exert effective interventions.

In conclusion, given the growing rate of stomach cancer incidence in specific geographical areas and, its high potential of mortality, and the possible relationship with environmental variables (e.g. climate variables); the efforts need to be focused on the identification of hot/cold spots, the predisposing factors, and the possible clusters in the affected areas.

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